



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,567	11/05/2001	Douglas F. Covey	WSHU 2044.1	6682

321 7590 11/26/2003

SENNIGER POWERS LEAVITT AND ROEDEL
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
----------	--------------

1625

DATE MAILED: 11/26/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/008,567	Applicant(s) COVEY, DOUGLAS F.	
	Examiner Evelyn Huang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-79 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 36-46 and 48-79 is/are rejected.
- 7) ☒ Claim(s) 38 and 47 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1625

DETAILED ACTION

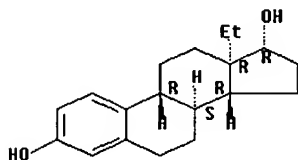
1. Claims 36-79 are pending. Claims 1-35 have been canceled according to the preliminary amendment filed on 4-7-2003.

Claim Rejections - 35 USC § 102

2. The rejection under 35 U.S.C. 102(b) as being anticipated by Romer I (Steroids, 1997, 62, pages 688-694, PTO-1449) is withdrawn in view of the amendment excluding the prior art compound.

3. The rejection under 35 U.S.C. 102(b) as being anticipated by GB 1 298 587 (PTO-1449) is withdrawn for claim 36 in view of the amendment excluding the prior art compound from the claim.

However, new claims 57, 58, 62, 64-66 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3) are subjected to this rejection because the following compound having a hydroxy on carbon 3 (page 6, column 1, lines 36-40, procedure B) is encompassed by the instant claims.



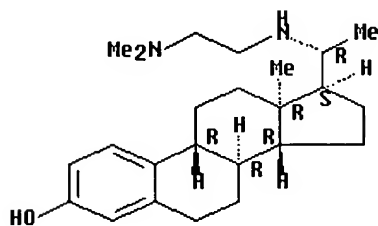
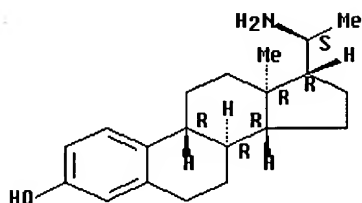
4. The rejection for Claim 36 under 35 U.S.C. 102(b) as being anticipated by Tietze (Steroids, 1994, 59, pages 305-309, PTO-1449) is withdrawn in view of the amendment excluding the prior art compound.

Art Unit: 1625

5. The rejection for Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Simpkins (WO 97/03661, PTO-1449) is withdrawn in view of the amendment excluding the prior art compound.

6. The rejection for Claim 36 under 35 U.S.C. 102(b) as being anticipated by Bonfils (5679668, PTO-1449) is withdrawn in view of the amendment excluding the prior art compounds.

The rejection, however, is maintained for new claims 57, 58, 62, 64, 65 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3), and claims 69, 70, 74-76 (wherein R^z on the D ring *may be* present on carbon 15, and/or 16, and therefore does not exclude substituent on carbon 17). The following compounds are encompassed by the instant claims wherein R^z at carbon 17 is substituted hydrocarbyl.



7. The rejection for Claim 36 under 35 U.S.C. 102(b) as being anticipated by Romer II (Steroids, 1997, 62, pages 304-310, PTO-1449) is withdrawn in view of the amendment excluding the prior art compounds.

Art Unit: 1625

The rejection, however, is maintained for new claims 57, 60, 62, 64-68 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3). In view of the disclosure that there may be more than one R^z (page 14 of the specification), the compounds, J 811, J835, J 861, J 851 (page 306, Figure 1) are encompassed by the instant claim wherein R^z is an attached ring structure, such as cycloalkyl, attached directly there to, as a fused ring (as defined on page 17 of the specification).

8. The rejection for Claims 36, 37, 39-44, 46 under 35 U.S.C. 102(b) as being anticipated by Lunn (Tetrahedron, 1968, 24(23), pages 6773-6776, PTO-1449) is withdrawn in view of the amendment excluding the prior art compound.

The rejection, however, is maintained for new claims 57, 61, 62, 64, 65, 68 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3), and claims 69, 70, 74-76 (wherein R^z on the D ring *may be* present on carbon 15, and/or 16, and therefore does not exclude substituent on carbon 17). Compound 5 having a hydroxy at carbon 3 and oxo at carbon 17 (Scheme I) is encompassed by the instant claims.

10. The rejection for Claims 36, 37, 39-44, 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Gemmill (5552395, PTO-1449) is withdrawn in view of the amendment excluding the prior art compounds.

The rejection, however, is maintained for new claims 57, 61, 62, 64, 65, 68 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3), and claims 69, 70, 74-76 (wherein R^z on the D ring *may be* present on carbon 15, and/or 16, and therefore does not exclude substituent on carbon 17). Compounds II (column 6), VI (column 7), VII, VIII (column 8), IV, I (column 9) having a hydroxy at carbon 3 and oxo at carbon 17 are encompassed by the instant claims.

Claim Rejections - 35 USC § 102(a)

11. The rejection for Claims 36, 39-47 under 35 U.S.C. 102(a) as being anticipated by DE 199 17 930 (PTO-1449) is withdrawn in view of the 131 Declaration by Mr. Covey providing evidence that the instant invention has been conceived and reduced to practice prior to October 19, 2000, the publication date of DE 199 17 930.

Claim Rejections - 35 USC § 112

12. The 35 U.S.C. 112, second paragraph rejection is maintained for reasons of record. The rejection is applicable to new claims 48, 51-54, 57-65, 67, 69-76, 78.

Applicant maintains that one of ordinary skill in the art would easily recognized 'amido' to mean "CONRR". However, the RR has not been described or defined in the specification, thereby rendering the claims indefinite.

While one of ordinary skill in the art knows the general meaning of a substituted or unsubstituted 'heterocycloalkyl' or 'heterocycloalkenyl', because the terms and the substituents on these groups are not found in the specification, the metes and bounds of the claims can not be ascertained.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-62, 64-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 49, 50, 56, 68, 79, the term 'spiro' has no antecedent basis in their respective base claims.

b. Claim 57, definition of 'n', 'may be' is not definite and is therefore unclear.

Art Unit: 1625

- c. Claim 69, definition of t, 'may be' is not definite and is therefore unclear.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 57-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is made assuming that for claim 57, the hydroxy substituents on the A ring are required to be present on carbon 1, 2 and/or 4 and for claim 69, the substituents on the D ring are required to be on carbon 15 and/or 16, as stated in Applicant's Remarks.

The subgenus of claims 57-68, wherein the hydroxy on ring A is on carbon 1, 2, and/or 4, has not been described in the specification, nor a species compound falling within this subgenus. The subgenus of claims 69-79, wherein the substituent on ring D is on carbon 15, and/or 16, has not been described in the specification, nor a species compound falling within this subgenus. The example compounds, ZYC-2, ZYC-4, do not have the double bonds or the configuration recited in these claims. The court has held that 'whatever may be the viability of an inductive-deductive approach to arriving at a claimed subgenus, it cannot be said that such a subgenus is necessarily described by a genus encompassing it and a species upon which it reads.' In re Wilder, 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984). See MPEP 2163.05.

Art Unit: 1625

Claim Rejections - 35 USC § 102(e)

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 57, 59, 60, 62, 64, 65, 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Droescher I (6436917). Droescher's anti-oxidative compounds (column 2, lines 47-50) are encompassed by the instant claims.

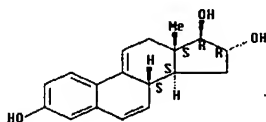
Claim Rejections - 35 USC § 102(b)

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

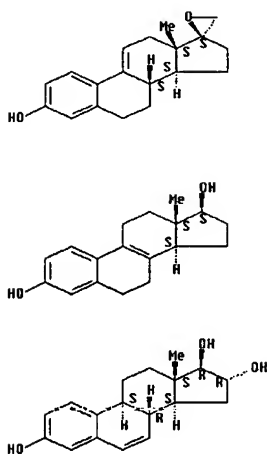
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 57, 59-62, 64-69, 71-78, 74-78 are rejected under 35 U.S.C. 102(b) as being anticipated by Droescher II (WO 95/13076, PTO-1449). The following compounds are encompassed by the instant claims 57, 59-62, 64-68 (wherein the hydroxy on the A ring *may be* present on carbon 1, 2 and/or 4, and therefore does not exclude hydroxy on carbon 3), and claims 69, 71-78, 74-76 (wherein R^z on the D ring *may be* present on carbon 15, and/or 16, and therefore does not exclude substituent on carbon 17).



Art Unit: 1625



Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. Claims 36, 37-46, 51-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gemmill (5552395, PTO-1440) or Romer II (Steroids, 1997, 62, pages 304-310, PTO-1449) or Driescher I (6436917) in view of Driescher II (WO 95/13076, PTO-1449).

Gemmill discloses 6, 8(9), 9(11)-dehydroestrone (columns 9-12) with antioxidant activity (column 16). Romer discloses a 8(9)-dehydroestrogen lipid peroxidation inhibiting compound (page 306, J 811, J 835). Driescher I discloses estradiol or 6, 8-pentaen- 1, 17-diol with anti-oxidant activity (columns 1-2; lines 47-50).

The compound of Gemmill, Romer, or Driescher has a different stereochemical configuration than the instant, which is the ent isomer of the prior art compound.

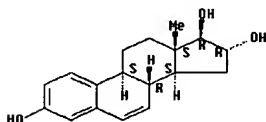
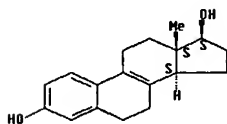
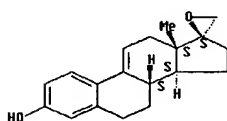
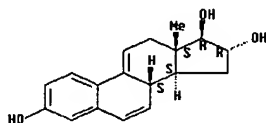
Driescher II teaches that Estradiol and ent-Estradiol have similar anti-oxidant activity although the ent isomer has a lower affinity for the estrogen receptor (Tables 1 and 2). In view of

Art Unit: 1625

Droescher's teaching, one of ordinary skill in the art would be motivated to prepare the ent isomer of Gemill, Romer or Droescher I to arrive at the instant invention with the reasonable expectation of having an additional compound having antioxidant activity with less estrogenic effect.

20. Claims 36, 37-46, 48, 51-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Droescher II (6172056).

Droescher II discloses dehydro-estradiol compounds with anti-oxidant activity (columns 1-2; lines 47-50).



The prior art compounds have a different stereochemical configuration than the instant, which is the ent isomer of the prior art compound.

Droescher II teaches that Estradiol and ent-Estradiol have similar anti-oxidant activity although the ent isomer has a lower affinity for the estrogen receptor (column 3, Table 1 and 2). In view of Droescher's teaching, one of ordinary skill in the art would be motivated to prepare

Art Unit: 1625

the ent isomer of Droesch II to arrive at the instant invention with the reasonable expectation of having an additional compound having antioxidant activity with less estrogenic effect.

Allowable Subject Matter

21. Claims 38, 47 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The compound of Tietze (Steroids, 1994, 59, pages 305-309, PTO-1449) or Romer II (Steroids, 1997, 62, pages 304-310, PTO-1449) has a different stereochemical configuration than the instant compound. Furthermore the prior art compound has a 17-hydroxy which is absent in the instant claim 38. Romer's compound has an oxo instead of the hydroxy of instant claim 47. Motivation to modify the prior art compound via multiple changes to arrive at the instant is lacking.

Conclusion

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

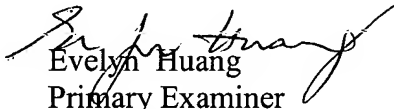
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1625

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
Art Unit 1625
